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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/759,152	01/16/2001	Michelle A.J. Palmer	4085-235-27 CIP	2836

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11/29/2002

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EXAMINER

ULM, JOHN D

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 11/29/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

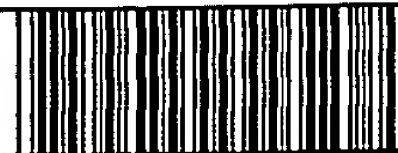
Office Action Summary

Application No.
09/759,152

Applicant(s)
Palmar et al.

Examiner
John Ulm

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sep 10, 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above, claim(s) 2-5, 11, 12, 14, 16, 17, and 19-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 6-10, 13, 15, 18, 24, and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on Sep 10, 2002 is/are a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other: _____

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1) Claims 1 to 25 are pending in the instant application. Claims 1, 6 to 9, 16 to 18, 20, 24 and 25 have been amended as requested by Applicant in Paper Number 12, filed 10 September 2002.

2) Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4) Claims 2 to 5 and 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

5) Claims 11, 12, 16, 17 and 19 to 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12. The traversal is on the premise that no undue search burden has been established because Applicant has already received an action on the merits. This has not been found persuasive because the original search for the plurality of different species of modified arrestins has proven burdensome. If Applicant wishes to concede, on the record, that any modified arrestin is obvious in view of any other modified arrestin for the purposes of the claimed invention then the requirement for an election of species will be withdrawn. Otherwise, the requirement is proper and made final.

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6) Claims 6 to 8 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for those reasons of record as applied to claims 1, 6 to 13 and 15 to 25 in section 7 of Paper Number 11. As stated therein, a critical element of the disclosed invention is the requirement that each member of a pair of interacting proteins be fused to one member of a pair of complementary β -galactosidase mutants. Applicant urges that the instant rejection is not applicable to the instant claims because they are drawn to compositions and not to methods. This is not found persuasive because the only method disclosed in the instant specification of using the claimed composition is when the "mutant form of a reporter enzyme" is complementary to a different mutant form of that enzyme such that the physical association of the two different forms of the mutant enzyme results in the restoration of enzymatic activity. The instant specification does not disclose how to use a DNA molecule of the instant claims which lacks this feature.

7) Claims 1, 6 to 10, 13 and 15, 18, 24 and 25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the Blau et al. patent (6,342,345 B1) in view of the Barak et al. patent (5,891,646, cited by Applicant) the Kovoov et al. publication (J. Biol. Chem. 274(11):6831-6834, 12 Mar. 1999, cited by Applicant), the Gurevich et al. '95 publication (J. Biol. Chem. 270(2):720-731, 13 Jan. 1995, cited by Applicant) and the Gurevich et al. '97 publication (Mol. Pharm. 51:161-169, 1997) for those reasons of record in section 10 of Paper Number 12. Applicant has traversed this rejection on the premise that there was no motivation to combine these references

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to arrive at the claimed invention. This premise is without foundation. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Barak et al. patent expressly and specifically disclosed the desirability of detecting the interaction of a ligand-activated G protein-coupled receptor with arrestin **in an intact cell** as a means of identifying compounds which can act as either agonist or antagonists of that receptor. The Blau et al. patent explicitly described a system for the detection of the molecular interaction between two proteins **in an intact cell** by expressing each of two those proteins as a fusion protein comprising one member of a pair of complementary β -galactosidase mutants, and expressly identified cell surface receptors as usable in the disclosed method. Finally, the Kovoov et al., Gurevich et al. '95 and the Gurevich et al. '97 publications were cited because they each described a variety of mutations which could be made to arrestins to render them either phosphorylation independent or to give them a higher affinity for a particular ligand-activated G protein-coupled receptor. Given that both of the Barak et al. and Blau et al. references teach methods for the detection of a specific protein-protein interaction in a living cell there was ample motivation to combine them. Since the Barak et al., Kovoov et al., Gurevich et al. '95 and the Gurevich et al. '97 all described the

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measurement of the interaction of arrestins with ligand-activated G protein-coupled receptors, an artisan would have certainly considered these references in combination.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant's argument that an artisan did not have a reasonable expectation that the interaction of a G protein-coupled receptor and an arrestin could be monitored by employing the complementation system of Blau et al. is without merit. Blau et al. is an issued U.S. patent. As such, it has a presumption of validity. The claims of Blau et al. encompass the claimed subject matter of the instant application in its entirety. Several of the claims in the Blau et al. patent expressly identify "members of a signal transduction cascade" and "cell surface receptors" as proteins with which the disclosed method can be practiced. To accept Applicant's argument that an artisan did not have a reasonable expectation that the interaction of a G protein-coupled receptor and an arrestin could be monitored by employing the complementation system of Blau et al. would require one to presume that the claims of Blau et al. are invalid under 35 U.S.C. § 112,

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first paragraph, and such a presumption, in the absence of clear and convincing evidence of inoperability, is prohibited by 35 U.S.C. § 282.

Applicant appears to be traversing the instant rejection on the basis that none of the cited references disclosed the claimed invention. Such arguments are clearly unpersuasive because the instant rejection is not based upon anticipation, it is based upon obviousness, which does not require that the prior art expressly disclose the claimed invention. The instant rejection is based upon the fact that all of the elements of the claimed invention are found in the references cited in conjunction with ample motivation to combine them in the manner claimed.

In response to applicant's argument that the method of measuring arrestin-receptor interaction employed by Barak et al. operates on a different principal than the method of measuring the interaction of two different proteins as taught by Blau et al., Applicant is advised that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

8) Applicant's arguments filed 10 September of 2002 have been fully considered but they are not persuasive for those reasons given above.

9) **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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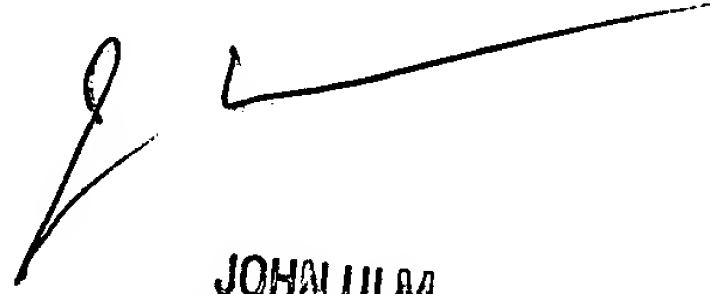
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



JOHN ULM
PRIMARY EXAMINER
GROUP 1600